```
=> d his

     (FILE 'HOME' ENTERED AT 17:58:57 ON 27 MAR 2002)

     FILE 'REGISTRY' ENTERED AT 17:59:05 ON 27 MAR 2002
L1                STRUCTURE UPLOADED
L2                QUE L1
L3             33 S L2
L4              1 S IBOGAMINE/CN
L5                SCREEN 963 AND 1006
L6                STRUCTURE UPLOADED
L7                QUE L6 AND L5
L8              9 S L7
L9            115 S L7 SSS FUL

     FILE 'CAPLUS' ENTERED AT 18:02:42 ON 27 MAR 2002
L10           405 S L9

     FILE 'REGISTRY' ENTERED AT 18:03:56 ON 27 MAR 2002
L11               SCREEN 963 AND 1006
L12               STRUCTURE UPLOADED
L13               QUE L12 AND L11
L14             1 S L13
L15            25 S L13 FUL SUB=L9

     FILE 'CAPLUS' ENTERED AT 18:05:43 ON 27 MAR 2002
L16           285 S L15

     FILE 'REGISTRY' ENTERED AT 18:05:55 ON 27 MAR 2002

     FILE 'CAPLUS' ENTERED AT 18:06:45 ON 27 MAR 2002

     FILE 'REGISTRY' ENTERED AT 18:06:58 ON 27 MAR 2002

     FILE 'CAPLUS' ENTERED AT 18:08:30 ON 27 MAR 2002
L17           ANALYZE L16 1- RN :    2640 TERMS

     FILE 'REGISTRY' ENTERED AT 18:09:17 ON 27 MAR 2002
L18              1 S 83-74-9/RN
                 SET NOTICE 1 DISPLAY
                 SET NOTICE LOGIN DISPLAY
L19            24 S L15 NOT L18

     FILE 'CAPLUS' ENTERED AT 18:09:53 ON 27 MAR 2002
L20            58 S L19

     FILE 'REGISTRY' ENTERED AT 18:12:04 ON 27 MAR 2002
L21               SCREEN 963 AND 1006
L22               STRUCTURE UPLOADED
L23               QUE L22 AND L21
L24             6 S L23 FUL SUB=L9

     FILE 'CAPLUS' ENTERED AT 18:12:43 ON 27 MAR 2002
L25            40 S L24

=> d 17
L7 HAS NO ANSWERS
L5                SCR 963 AND 1006
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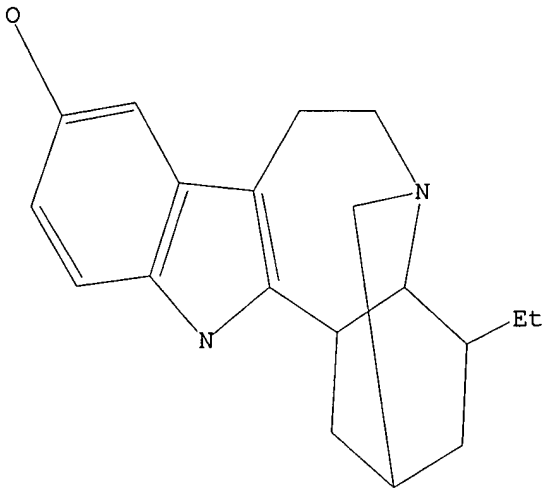
L6 STR



Structure attributes must be viewed using STN Express query preparation.
L7 QUE ABB=ON PLU=ON L6 AND L5

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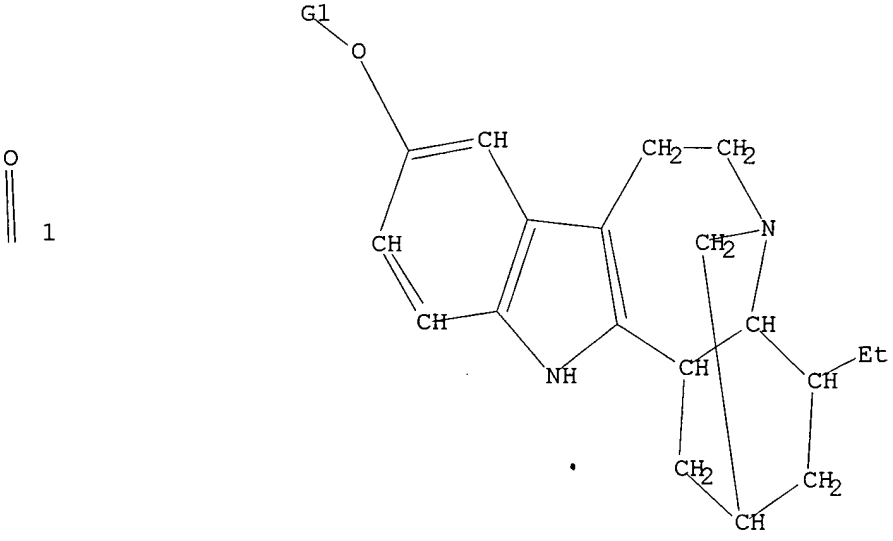
L23 HAS NO ANSWERS
L21 SCR 963 AND 1006
L22 STR



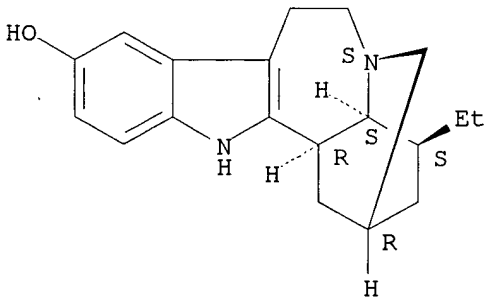
G1 H,[@1]

Structure attributes must be viewed using STN Express query preparation.
L23 QUE ABB=ON PLU=ON L22 AND L21

=> d bib abs hitstr l25 1-40

L25 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2001:757619 CAPLUS
DN 136:111976
TI Ibogaine in the treatment of heroin withdrawal
AU Mash, Deborah C.; Kovera, Craig A.; Pablo, John; Tyndale, Rachel; Ervin, Frank R.; Kamlet, Jeffrey D.; Hearn, W. Lee
CS Departments of Neurology and Pharmacology, University of Miami School of Medicine, Miami, FL, 33124, USA
SO Alkaloids (Academic Press) (2001), 56(Ibogaine), 155-171
CODEN: ALKAAR; ISSN: 0099-9598
PB Academic Press
DT Journal; General Review
LA English
AB A review describes ibogaine treatment as a novel approach to reduce the time it takes to complete the process of detoxification or to further reduce persisting subjective reports of dysphoria and opiate craving. Pharmacol. treatments for heroin addiction currently employ two strategies, i.e., detoxification followed by drug-free abstinence or maintenance treatment with an opioid agonist. Ibogaine treatment has similarities with other detoxification pharmacotherapies, including substitution with a longer-acting opiate, e.g., methadone or buprenorphine. However, ibogaine appears to be a prodrug with the beneficial effects residing in the active metabolite noribogaine. Thus, noribogaine alone is effective in detoxification of heroin-dependent and methadone-maintained patients. (c) 2001 Academic Press.
IT **481-88-9**, Noribogaine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibogaine in heroin withdrawal treatment)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

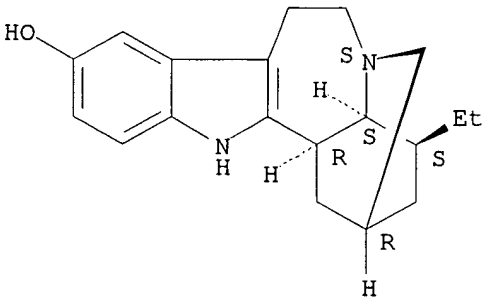
Absolute stereochemistry.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2001:757617 CAPLUS
DN 136:111974
TI Comparative neuropharmacology of ibogaine and its O-desmethyl metabolite, noribogaine
AU Baumann, Michael H.; Pablo, John; Ali, Syed F.; Rothman, Richard B.; Mash, Deborah C.
CS Clinical Psychopharmacology Section Intramural Research Program National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, 21224, USA
SO Alkaloids (Academic Press) (2001), 56(Ibogaine), 79-113
CODEN: ALKAAR; ISSN: 0099-9598
PB Academic Press
DT Journal; General Review
LA English
AB A review, on the comparative neurobiol. of ibogaine and noribogaine in rodent species. The data presented showed that ibogaine interacts with multiple neurotransmitter systems known to modulate drug addiction. The in vitro pharmacol. activity of ibogaine is further complicated by the metabolic conversion of ibogaine to its active O-desmethyl metabolite, noribogaine, in rats, monkeys, and humans. Noribogaine might contribute to the antiaddictive properties of systematically administered ibogaine. It might also be the active compd. mediating the long-term actions of ibogaine. (c) 2001 Academic Press.
IT **481-88-9**, Noribogaine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative neuropharmacol. of ibogaine and its O-desmethyl metabolite, noribogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

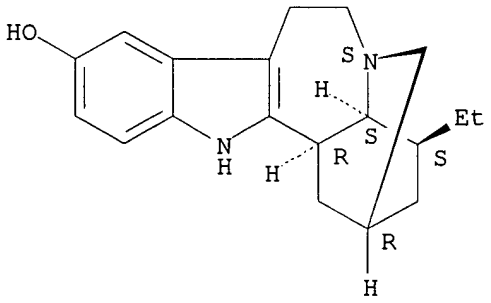
Absolute stereochemistry.



RE.CNT 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2001:321619 CAPLUS
DN 135:132300
TI In vivo neurobiological effects of ibogaine and its O-desmethyl metabolite, 12-hydroxyibogamine (noribogaine), in rats
AU Baumann, Michael H.; Rothman, Richard B.; Pablo, John P.; Mash, Deborah C.
CS Clinical Psychopharmacology Section, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(2), 531-539
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Ibogaine is a naturally occurring compd. with purported antiaddictive properties. When administered to primates, ibogaine is rapidly o-demethylated to form the metabolite 12-hydroxyibogamine (noribogaine). Peak blood levels of noribogaine exceed those of ibogaine, and noribogaine persists in the bloodstream for at least 1 day. Very few studies have systematically evaluated the neurobiol. effects of noribogaine in vivo. In the present series of expts., we compared the effects of i.v. administration of ibogaine and noribogaine (1 and 10 mg/kg) on motor behaviors, stress hormones, and extracellular levels of dopamine (DA) and serotonin (5-HT) in the nucleus accumbens of male rats. Ibogaine caused dose-related increases in tremors, whereas noribogaine did not. Both ibogaine and noribogaine produced significant elevations in plasma corticosterone and prolactin, but ibogaine was a more potent stimulator of corticosterone secretion. Neither drug altered extracellular DA levels in the nucleus accumbens. However, both drugs increased extracellular 5-HT levels, and noribogaine was more potent in this respect. Results from in vitro expts. indicated that ibogaine and noribogaine interact with 5-HT transporters to inhibit 5-HT uptake. The present findings demonstrate that noribogaine is biol. active and undoubtedly contributes to the in vivo pharmacol. profile of ibogaine in rats. Noribogaine is approx. 10 times more potent than ibogaine as an indirect 5-HT agonist. More importantly, noribogaine appears less apt to produce the adverse effects assocd. with ibogaine, indicating the metabolite may be a safer alternative for medication development.
IT **481-88-9**, Noribogaine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vivo neurobiol. effects of ibogaine and its O-desmethyl metabolite, 12-hydroxyibogamine (noribogaine), in rats)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

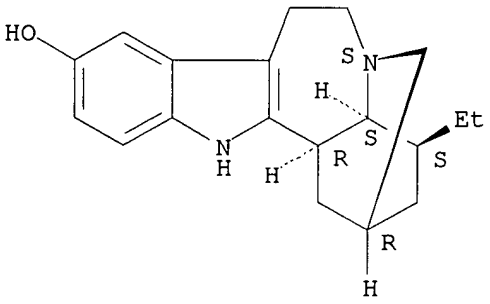
Absolute stereochemistry.



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

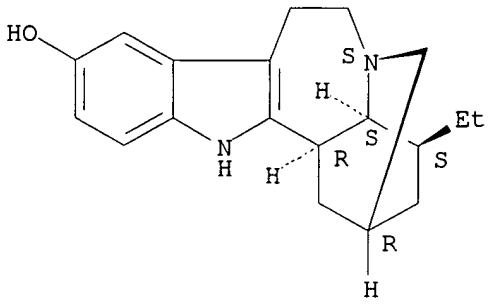
L25 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2001:264421 CAPLUS
DN 135:40900
TI Noribogaine: an active metabolite of the indole alkaloid ibogaine as an anti-addiction pharmacotherapy
AU Pablo, John P.
CS Univ. of Miami, Coral Gables, FL, USA
SO (2000) 140 pp. Avail.: UMI, Order No. DA9972552
From: Diss. Abstr. Int., B 2000, 61(5), 2409
DT Dissertation
LA English
AB Unavailable
IT **481-88-9**, Noribogaine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ibogaine indole alkaloid metabolite noribogaine as anti-addiction pharmacotherapy)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2000:842753 CAPLUS
DN 134:360947
TI Ibogaine: Complex pharmacokinetics, concerns for safety, and preliminary efficacy measures
AU Mash, Deborah C.; Kovera, Craig A.; Pablo, John; Tyndale, Rachel F.; Ervin, Frank D.; Williams, Izben C.; Singleton, Edward G.; Mayor, Manny
CS Department of Neurology, University of Miami School of Medicine, Miami, FL, 33136, USA
SO Annals of the New York Academy of Sciences (2000), 914(Neurobiological Mechanisms of Drugs of Abuse), 394-401
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB Ibogaine is an indole alkaloid found in the roots of Tabernanthe Iboga (Apocynaceae family), a rain forest shrub that is native to western Africa. Ibogaine is used by indigenous peoples in low doses to combat fatigue, hunger, and thirst, and in higher doses as a sacrament in religious rituals. Members of American and European addict self-help groups have claimed that ibogaine promotes long-term drug abstinence from addictive substances, including psychostimulants, and opiates. Anecdotal reports attest that a single dose of ibogaine eliminates opiate withdrawal symptoms and reduces drug craving for extended periods of time. The purported efficacy of ibogaine for the treatment of drug dependence may be due in part to an active metabolite. The majority of ibogaine biotransformation proceeds via CYP2D6, including the O-demethylation of ibogaine to 12-hydroxyibogamine (noribogaine). Blood concn.-time effect profiles of ibogaine and noribogaine obtained for individual subjects after single oral dose administrations demonstrate complex pharmacokinetic profiles. Ibogaine has shown preliminary efficacy for opiate detoxification and for short-term stabilization of drug-dependent persons as they prep. to enter substance abuse treatment. The authors report here that ibogaine decreased craving for cocaine and heroin during inpatient detoxification. Self-reports of depressive symptoms were also lower after ibogaine treatment and at 30 days after program discharge. Because ibogaine is cleared rapidly from the blood, the beneficial aftereffects of the drug on craving and depressed mood may be related to the effects of noribogaine on the central nervous system.
IT **481-88-9**, Noribogaine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(anti-addictive agent ibogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

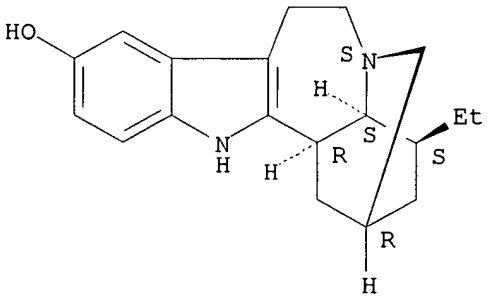
Absolute stereochemistry.



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2000:842750 CAPLUS
DN 134:361267
TI Noribogaine (12-hydroxyibogamine): A biologically active metabolite of the antiaddictive drug ibogaine
AU Baumann, M. H.; Pablo, J. P.; Ali, S. F.; Rothman, R. B.; Mash, D. C.
CS Clinical Psychopharmacology Section, Intramural Research Program, NIDA, NIH, Baltimore, MD, 21224, USA
SO Annals of the New York Academy of Sciences (2000), 914(Neurobiological Mechanisms of Drugs of Abuse), 354-368
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB Ibogaine (IBO) is a plant-derived alkaloid that is being evaluated as a possible medication for substance use disorders. When administered peripherally to monkeys and humans, IBO is rapidly converted to an o-demethylated metabolite, 12-hydroxyibogamine (NORIBO). We have found in rats that peak blood levels of NORIBO can exceed those of the parent compd., and NORIBO persists in the bloodstream for at least 24 h. Surprisingly few studies have examd. the in vivo biol. activity of NORIBO. In the present series of expts., we compared the effects of i.v. administration of IBO and NORIBO (1 and 10 mg/kg) on unconditioned behaviors, circulating stress hormones, and extracellular levels of dopamine (DA) and serotonin (5-HT) in the nucleus accumbens of male rats. IBO caused dose-related increases in tremors and forepaw treading, whereas NORIBO did not. Both IBO and NORIBO produced significant elevations in plasma corticosterone and prolactin, but IBO was more potent as a stimulator of corticosterone secretion. Neither drug affected extracellular DA levels in the nucleus accumbens. However, both IBO and NORIBO increased extracellular 5-HT levels, and NORIBO was more potent in this regard. The present data demonstrate that NORIBO is biol. active and undoubtedly contributes to the in vivo pharmacol. profile of IBO in rats. Most importantly, NORIBO appears less likely to produce the adverse effects assocd. with IBO (i.e., tremors and stress-axis activation), suggesting that the metabolite may be a safer alternative for medication development.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(noribogaine: a biol. active metabolite of antiaddictive drug ibogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

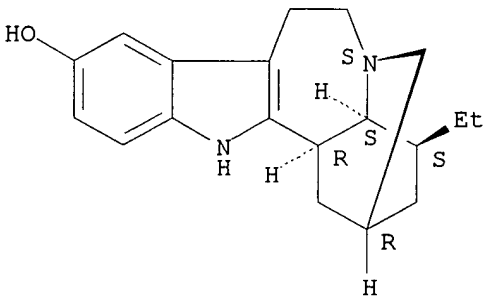
Absolute stereochemistry.



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2000:716746 CAPLUS
DN 134:231357
TI Ibogaine and noribogaine: comparing parent compound to metabolite
AU Zubaran, Carlos
CS Department of Biochemistry, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
SO CNS Drug Reviews (2000), 6(3), 219-240
CODEN: CDREFB; ISSN: 1080-563X
PB Neva Press
DT Journal; General Review
LA English
AB A review with 112 refs. Ibogaine is one of the psychoactive alkaloids found in the West African shrub Tabernanthe iboga. Since the 1980s, a series of US patents have claimed efficacy for ibogaine in the treatment of drug addiction. Since then, >60 scientific publications on ibogaine and drug addiction have been published. Ibogaine has an acute and a prolonged effect on neurochem. and behavior. Its metabolite, noribogaine (12-hydroxyibogamine), is produced through metabolic demethylation soon after oral ibogaine administration. Although they share similar chem. structures, ibogaine and noribogaine display different binding profiles. In rodents, both ibogaine and noribogaine decreased morphine and cocaine intake and modulated dopaminergic transmission. In rats trained to discriminate ibogaine from saline, complete generalization to noribogaine was obtained. Attempts to correlate brain levels of both the parent compd. and the metabolite indicate that noribogaine is primarily responsible for ibogaine's discriminative-stimulus effects. Ibogaine-induced neurotoxicity tends to occur at doses much higher than the proposed dose for humans, but caution is important when extrapolating data from ibogaine's effects in rodents. Although a definitive clin. validation of purported ibogaine effects is still unavailable, ibogaine has opened new perspectives in the investigation of pharmacotherapies for drug addiction.
IT **481-88-9**, Noribogaine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(pharmacol. of ibogaine and its metabolite noribogaine with respect to treatment of drug addiction)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

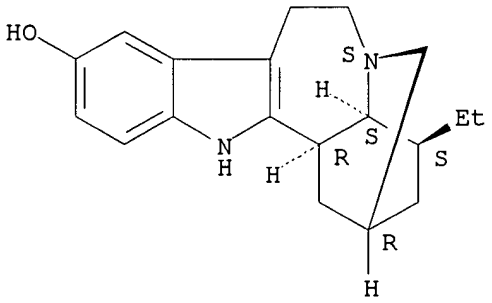
Absolute stereochemistry.



RE.CNT 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2000:547065 CAPLUS
DN 134:405
TI Development of novel medications for drug addiction. The legacy of an African shrub
AU Glick, Stanley D.; Maisonneuve, Isabelle M.
CS Department of Pharmacology and Neuroscience, Albany Medical College, Albany, NY, 12208, USA
SO Annals of the New York Academy of Sciences (2000), 909(New Medications for Drug Abuse), 88-103
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB Ibogaine, one of several alkaloids found in the root bark of the African shrub Tabernanthe iboga, has been claimed to be effective in treating multiple forms of drug abuse. Problems assocd. with side effects of ibogaine have spawned a search for more effective and safer structural derivs. 18-Methoxycoronaridine (18-MC), a novel iboga alkaloid congener, appears to have substantial potential for broad use as an antiaddictive therapy. Like ibogaine (40 mg/kg), 18-MC (40 mg/kg) decreased the i.v. self-administration of morphine and cocaine and the oral self-administration of EtOH and nicotine in rats; unlike ibogaine, 18-MC did not affect responding for a nondrug reinforcer (water). Ibogaine and 18-MC appear to reduce the reinforcing efficacies, rather than the potencies, of drugs of abuse. Both ibogaine and 18-MC decreased extracellular levels of dopamine in the rat nucleus accumbens, while only ibogaine increased serotonin levels in this brain region. Both ibogaine and 18-MC blocked morphine-induced and nicotine-induced dopamine release in the accumbens; only ibogaine enhanced cocaine-induced increases in dopamine. Ibogaine produced whole-body tremors and, at high doses (.gtoreq.100 mg/kg), cerebellar damage; 18-MC did not produce these effects. Ibogaine, but not 18-MC, caused bradycardia at high doses. Ibogaine and its metabolite noribogaine had low-.mu.M affinities for .kappa. and .mu. opioid receptors, NMDA receptors, 5HT3 receptors, .sigma.-2 sites, sodium channels and the serotonin transporter. 18-MC had low-.mu.M affinities at all three opioid receptors and at 5HT3 receptors but much lower or no affinities for NMDA and .sigma.-2 receptors, sodium channels, and the serotonin transporter. Both 18-MC and ibogaine were sequestered in fat; like ibogaine, 18-MC probably has an active metabolite. 18-MC also has (+) and (-) enantiomers, both of which are active. The data indicate that 18-MC should be safer than ibogaine and at least as effective as an antiaddictive drug.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ibogaine, noribogaine and methoxycoronaridine binding to brain receptors)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

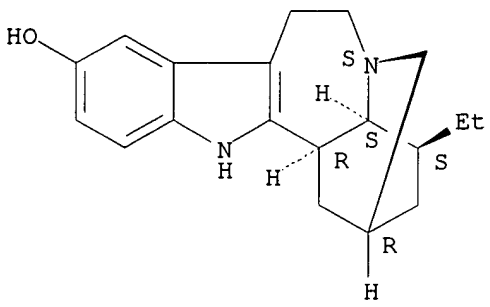
Absolute stereochemistry.



RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 2000:171768 CAPLUS
DN 132:318283
TI Modulation of cellular calcium by sigma-2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells
AU Vilner, Bertold J.; Bowen, Wayne D.
CS Unit on Receptor Biochemistry and Pharmacology, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA
SO J. Pharmacol. Exp. Ther. (2000), 292(3), 900-911
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Human SK-N-SH neuroblastoma cells expressed sigma-1 and sigma-2 receptors with similar pharmacol. profiles to those of rodent-derived tissues, although sigma-2 receptors exhibited some affinity differences that might suggest heterogeneity or species differences. Structurally diverse sigma ligands produced two types of increases in intracellular (cytosolic) Ca2+ concn. ([Ca2+]i) in these cells. CB-64D, CB-64L, JL-II-147, BD737, LR172, BD1008, haloperidol, reduced haloperidol, and ibogaine all produced an immediate, dose-dependent, and transient rise in [Ca2+]i. Sigma-inactive compds. structurally similar to the most active sigma ligands and ligands for several neurotransmitter receptors produced little or no effect. The high activity of CB-64D and ibogaine (sigma-2-selective ligands) compared with the low activity of (+)-pentazocine and other (+)-benzomorphans (sigma-1-selective ligands), in addn. to enantioselectivity for CB-64D over CB-64L, strongly indicated mediation by sigma-2 receptors. The effect of CB-64D and BD737 was blocked by the sigma antagonists BD1047 and BD1063, further confirming specificity as a receptor-mediated event. The transient rise in [Ca2+]i occurred in the absence of extracellular Ca2+ and was completely eliminated by pretreatment of cells with thapsigargin. Thus, sigma-2 receptors stimulate a transient release of Ca2+ from the endoplasmic reticulum. Prolonged exposure of cells to sigma-receptor ligands resulted in a latent and sustained rise in [Ca2+]i, with a pharmacol. profile identical to that of the transient rise. This sustained rise in [Ca2+]i was affected by neither the removal of extracellular Ca2+ nor thapsigargin pretreatment, suggesting latent sigma-2 receptor-induced release from thapsigargin-insensitive intracellular Ca2+ stores. Sigma-2 receptors may use Ca2+ signals in producing cellular effects.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(modulation of cellular calcium by .sigma.-2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.


HO
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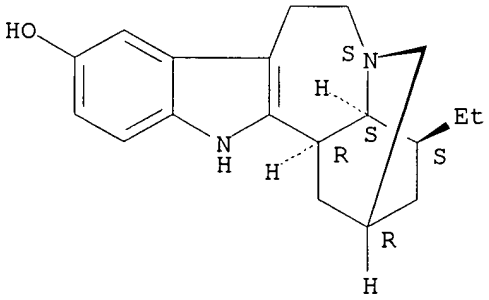
L25 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1999:430105 CAPLUS
DN 131:252403
TI Noribogaine generalization to the ibogaine stimulus: correlation with noribogaine concentration in rat brain
AU Zubaran, C.; Shoaid, M.; Stolerman, I. P.; Pablo, J.; Mash, D. C.
CS Section of Behavioural Pharmacology, Institute of Psychiatry, London, SE5 8AF, UK
SO Neuropsychopharmacology (1999), 21(1), 119-126
CODEN: NEROEW; ISSN: 0893-133X
PB Elsevier Science Inc.
DT Journal
LA English
AB The discriminative stimulus effects of ibogaine and noribogaine in rats have been examd. in relation to their concns. in blood plasma and brain regions and to receptor systems through which they have been proposed to act. Rats were trained to discriminate ibogaine (10 mg/kg IP), the NMDA antagonist dizocilpine (0.08 mg/kg IP) or the .kappa.-opioid agonist U50,488 (5 mg/kg IP) from vehicle in a std. two-lever operant conditioning procedure with a tandem VI-FR schedule of food reinforcement. Only rats trained on ibogaine generalized to noribogaine, which was approx. twice as potent as the parent compd. Noribogaine was detected in plasma and brain after administration of ibogaine and noribogaine. At the ED50 doses for the discriminative effect, the estd. concns. of noribogaine in plasma, cerebral cortex, and striatum were similar regardless of whether ibogaine or noribogaine was administered. The findings suggest that the metabolite noribogaine may be devoid of NMDA antagonist and .kappa.-opioid agonist discriminative effects and that it may play a major role in mediating the discriminative stimulus effect of ibogaine.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(noribogaine generalization to ibogaine stimulus and correlation with noribogaine concn. in rat brain)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1999:184122 CAPLUS
DN 130:205166
TI Noribogaine in the treatment of pain and drug addiction
IN Mash, Deborah C.
PA Novoneuron, Inc., USA
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

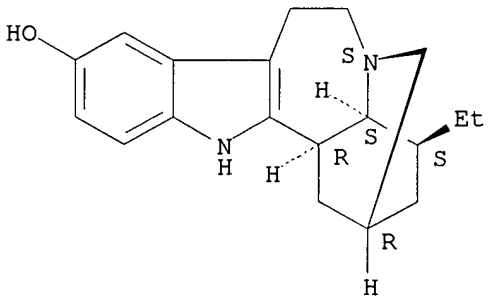
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911250	A2	19990311	WO 1998-US18284	19980903
	WO 9911250	A3	19990805		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9892174	A1	19990322	AU 1998-92174	19980903
	EP 1009407	A2	20000621	EP 1998-944698	19980903
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	US 1997-57921P	P	19970904		
	WO 1998-US18284	W	19980903		

AB The present invention is directed to methods of treating patients for pain by administering noribogaine. Noribogaine may also be used to treat patients for the symptoms assocd. with withdrawal from drug dependency. In the latter case, the noribogaine treatment should be supplemented with the administration of an opioid antagonist such as naloxone.

IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noribogaine and opioid antagonists for treatment of pain and drug addiction)

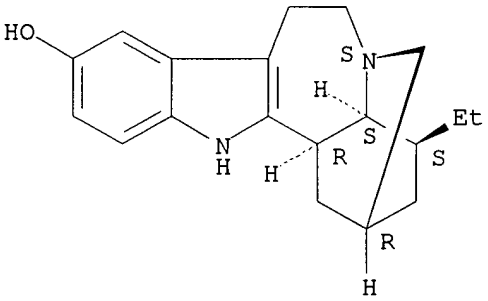
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



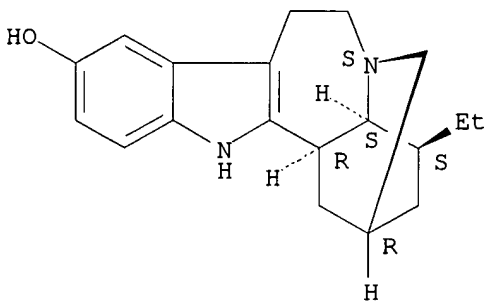
L25 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:656503 CAPLUS
DN 129:270563
TI Enhancement of morphine antinociception by ibogaine and noribogaine in morphine-tolerant mice
AU Sharma, Shyam Sunder; Bhargava, Hemendra N.
CS Department Pharmaceutics Pharmacodynamics (M/C 865), Health Sciences Center, University Illinois, Chicago, IL, 60612, USA
SO Pharmacology (1998), 57(5), 229-232
CODEN: PHMGBN; ISSN: 0031-7012
PB S. Karger AG
DT Journal
LA English
AB The effects of ibogaine, an alkaloid isolated form the bark of the African shrub, Tabernathe iboga, and noribogaine, a metabolite of ibogaine, on morphine antinociception were detd. in male Swiss-Webster mice. Mice were rendered tolerant to morphine by implanting them with a pellet contg. 25 mg of morphine base for 3 days. Placebo pellet-implanted mice served as controls. The antinociception of morphine (10 mg/kg, s.c.) was detd. alone or in combination with an appropriate dose of ibogaine or noribogaine. Tolerance to morphine developed as a result of morphine pellet implantation as evidenced by decreased antinociceptive response to morphine. Both ibogaine and noribogaine dose-dependently enhanced morphine antinociception in morphine-tolerant but not in morphine-naive mice. It is concluded that ibogaine and noribogaine enhance morphine antinociception in morphine-tolerant mice.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of morphine antinociception by ibogaine and noribogaine in morphine-tolerant mice)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:540906 CAPLUS
DN 129:225279
TI Cytochrome P 450 2D6 catalyzes the O-demethylation of the psychoactive alkaloid ibogaine to 12-hydroxyibogamine
AU Obach, R. Scott; Pablo, John; Mash, Deborah C.
CS Central Research Division, Department of Drug Metabolism, Groton, CT, 06340, USA
SO Drug Metab. Dispos. (1998), 26(8), 764-768
CODEN: DMDSAI; ISSN: 0090-9556
PB Williams & Wilkins
DT Journal
LA English
AB Ibogaine is a psychoactive alkaloid that possesses potential as an agent to treat opiate and cocaine addiction. The primary metabolite arises via O-demethylation at the 12-position to yield 12-hydroxyibogamine. Evidence is presented that the O-demethylation of ibogaine obsd. in human hepatic microsomes is catalyzed primarily by the polymorphically expressed cytochrome P 450 2D6 (CYP2D6). An enzyme kinetic examn. of ibogaine O-demethylase activity in pooled human liver microsomes suggested that 2 (or more) enzymes are involved in this reaction: one with a low KMapp (1.1 .mu.M) and the other with a high KMapp (>200 .mu.M). The low KMapp activity comprised >95% of total intrinsic clearance. Human liver microsomes from 3 individual donors demonstrated similar enzyme kinetic parameters (mean KMapp = 0.55 .+-. 0.09 .mu.M and 310 .+-. 10 .mu.M for low and high KM activities, resp.). However, a 4th human microsome sample that appeared to be a phenotypic CYP2D6 poor metabolizer possessed only the high KMapp activity. In hepatic microsomes from a panel of human donors, the low KMapp ibogaine O-demethylase activity correlated with CYP2D6-catalyzed bufuralol 1'-hydroxylase activity but not with other P 450 isoform-specific activities. Quinidine, a CYP2D6-specific inhibitor, inhibited ibogaine O-demethylase (IC50 = 0.2 .mu.M), whereas other P 450 isoform-specific inhibitors did not inhibit this activity. Also, of a battery of recombinant heterologously expressed human P 450 isoforms, only rCYP2D6 possessed significant ibogaine O-demethylase activity. Thus, it is concluded that ibogaine O-demethylase is catalyzed by CYP2D6 and that this isoform is the predominant enzyme of ibogaine O-demethylation in humans. The potential pharmacol. implications of these findings are discussed.
IT **481-88-9**, 12-Hydroxyibogamine
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(O-demethylation of psychoactive alkaloid ibogaine to 12-hydroxyibogamine catalyzed by cytochrome P 4502D6)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.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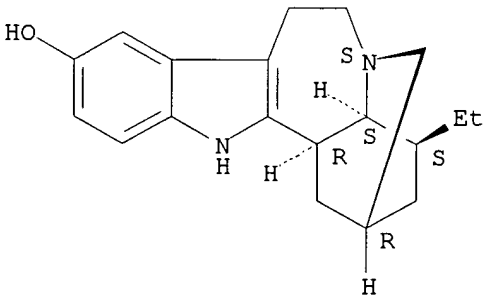
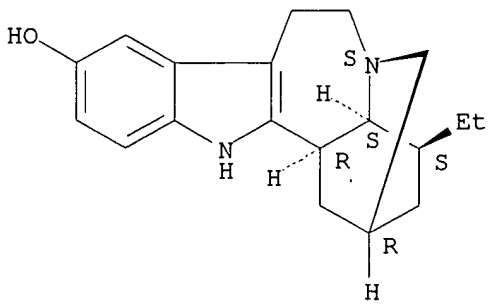
L25 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:469623 CAPLUS
DN 129:170461
TI Medication development of ibogaine as a pharmacotherapy for drug dependence
AU Mash, Deborah C.; Kovera, Craig A.; Buck, Billy E.; Norenberg, Michael D.; Shapshak, Paul; Hearn, W. Lee; Sanchez-Ramos, Juan
CS Departments of Neurology, Psychiatry, Orthopedics, and Pathology, University of Miami School of Medicine, Miami, FL, 33136, USA
SO Ann. N. Y. Acad. Sci. (1998), 844(Neurochemistry of Drugs of Abuse), 274-292
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
AB The potential for deriving new psychotherapeutic medications from natural sources has led to renewed interest in rain forest plants as a source of lead compds. for the development of antiaddiction medications. Ibogaine is an indole alkaloid found in the roots of Tabernanthe iboga. Ibogaine is used by indigenous peoples in low doses to combat fatigue, hunger, and in higher doses as a sacrament in religious rituals. Members of American and European addict self-help groups have claimed that ibogaine promotes long-term drug abstinence from addictive substances, including psychostimulants and cocaine. Anecdotal reports attest that a single dose of ibogaine eliminates withdrawal symptoms and reduces drug cravings for extended periods of time. The purported antiaddictive properties of ibogaine require rigorous validation in humans. We have initiated a rising tolerance study using single administration to assess the safety of ibogaine for the treatment of cocaine dependency. The primary objectives of the study are to det. safety, pharmacokinetics and dose effects, and to identify relevant parameters of efficacy in cocaine-dependent patients. Pharmacokinetic and pharmacodynamic characteristics of ibogaine in humans are assessed by analyzing the concn.-time data of ibogaine and its desmethyl metabolite (noribogaine) from the phase I trial, and by conducting in vitro expts. to elucidate the specific disposition processes involved in the metab. of both parent drug and metabolite. A review of ibogaine use and effects is added.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(ibogaine, pharmacokinetics and use in the pharmacotherapy for drug dependence)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:469618 CAPLUS
DN 129:239769
TI Mechanisms of antiaddictive actions of ibogaine
AU Glick, Stanley D.; Maisonneuve, Isabelle M.
CS Department of Pharmacology and Neuroscience, A-136, Albany Medical College, Albany, NY, 12208, USA
SO Ann. N. Y. Acad. Sci. (1998), 844(Neurochemistry of Drugs of Abuse), 214-226
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB Ibogaine, an alkaloid extd. from Tabemanthe iboga, is being studied as a potential long-acting treatment for opioid and stimulant abuse as well as for alcoholism and smoking. Studies in this lab. have used animal models to characterize ibogaine's interactions with drugs of abuse, and to investigate the mechanisms responsible. Ibogaine, as well as its metabolite, noribogaine, can decrease both morphine and cocaine self-administration for several days in some rats; shorter-lasting effects appear to occur on ethanol and nicotine intake. Acutely, both ibogaine and noribogaine decrease extra-cellular levels of dopamine in the nucleus accumbens of the rat brain. Ibogaine pretreatment (19 h beforehand) blocks morphine-induced dopamine release and morphine-induced locomotor hyperactivity while, in contrast, it enhances similar effects of stimulants (cocaine and amphetamine). Ibogaine pretreatment also blocks nicotine-induced dopamine release. Both ibogaine and noribogaine bind to kappa opioid and N-methyl-D-aspartate (NMDA) receptors and to serotonin uptake sites; ibogaine also binds to sigma-2 and nicotinic receptors. The relative contributions of these actions are being assessed. Our ongoing studies in rats suggest that kappa agonist and NMDA antagonist actions contribute to ibogaine's effects on opioid and stimulant self-administration, while the serotonergic actions may be more important for ibogaine-induced decreases in alc. intake. A nicotinic antagonist action may mediate ibogaine-induced redn. of nicotine preferences in rats. A sigma-2 action of ibogaine appears to mediate its neurotoxicity. Some effects of ibogaine (e.g., on morphine and cocaine self-administration, morphine-induced hyperactivity, cocaine-induced increases in nucleus accumbens dopamine) are mimicked by a kappa agonist (U50,488) and/or a NMDA antagonist (MK-801). Moreover, a combination of a kappa antagonist and a NMDA agonist will partially reverse several of ibogaine's effects. Ibogaine's long-term effects may be mediated by slow release from fat tissue (where ibogaine is sequestered) and conversion to noribogaine. Different receptors, or combinations of receptors, may mediate interactions of ibogaine with different drugs of abuse.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(mechanisms of antiaddictive actions of ibogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.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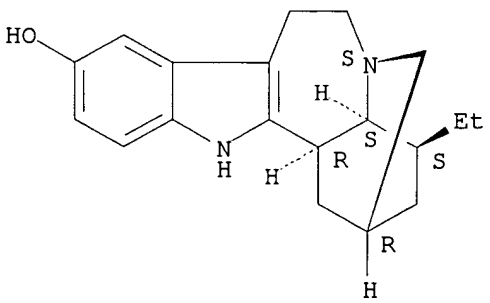
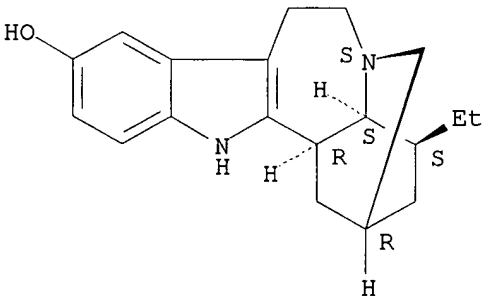
L25 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:466864 CAPLUS
DN 129:211558
TI Acute iboga alkaloid effects on extracellular serotonin (5-HT) levels in nucleus accumbens and striatum in rats
AU Wei, D.; Maisonneuve, I. M.; Kuehne, M. E.; Glick, S. D.
CS Department of Pathology and Laboratory Medicine, Albany Medical College, Albany, NY, 12208, USA
SO Brain Res. (1998), 800(2), 260-268
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB The iboga alkaloid, ibogaine, its metabolite, noribogaine, and the congener, 18-methoxycoronaridine (18-MC) have all been claimed to have anti-addictive properties in animal models, but the mechanisms underlying these effects are unclear. Ibogaine and noribogaine were shown to have affinity for the serotonin transporter, and inhibition of serotonin reuptake has been proposed to be involved in their anti-addictive actions. It is not known yet if 18-MC also has this property. In vivo microdialysis and HPLC (microbore) were used to det. acute changes in extracellular serotonin levels in nucleus accumbens (NAC) and striatum (STR) after both i.p. (40 mg/kg for all drugs) and i.v. (1-10 mg/kg for ibogaine and noribogaine) drug administration in awake freely moving female Sprague-Dawley rats (250-275 g). After i.p. administration, ibogaine, noribogaine and 18-MC had very different effects on extracellular serotonin levels in both NAC and STR: ibogaine elicited large increases (up to 25-fold in NAC and 10- fold in STR), noribogaine produced moderate increases (up to 8-fold in NAC and 5-fold in STR), and 18-MC had no effect in either brain region. These and other data suggest that (1) the serotonergic system may not be an essential factor in the anti-addictive actions of these drugs; (2) ibogaine (or an unidentified metabolite) may release serotonin as well as inhibit its reuptake; (3) stimulation of the ascending serotonergic system may mediate ibogaine's hallucinogenic effect; and (4) 18-MC probably has no affinity for the serotonin transporter, and is unlikely to be a hallucinogen.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(iboga alkaloid effects on extracellular serotonin in nucleus accumbens and striatum in rats)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



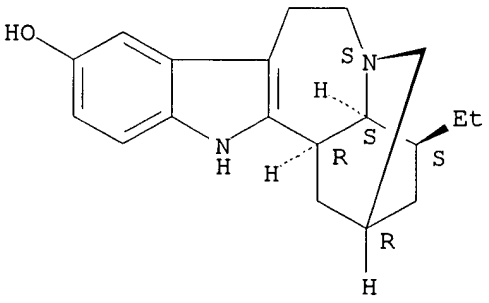
L25 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:108539 CAPLUS
DN 128:200970
TI Noribogaine stimulates naloxone-sensitive [35S]GTP.gamma.S binding
AU Pablo, John P.; Mash, Deborah C.
CS Departments of Neurology (D4-5) and Molecular and Cellular Pharmacology, University of Miami School of Medicine, Miami, FL, USA
SO NeuroReport (1998), 9(1), 109-114
CODEN: NERPEZ; ISSN: 0959-4965
PB Rapid Science Publishers
DT Journal
LA English
AB Noribogaine is formed in vivo by the O-demethylation of the indole alkaloid ibogaine. We report here that noribogaine acts as a full agonist at the .mu.-opioid receptor. Noribogaine-stimulated guanylyl 5'.gamma.-[35S]thio-triphosphate ([35S]GTP.gamma.S) was studied in rat thalamic membranes to measure activation of guanine nucleotide binding proteins (G-proteins) in the presence of excess GDP. Noribogaine caused a 170% increase above basal [35S]GTP.gamma.S binding at sub-micromolar effective concns. (EC50) in a naloxone-sensitive manner, confirming that this effect was an opioid receptor-mediated process. The level of intrinsic activity for noribogaine in these assays was comparable to the full agonists DAMGO and morphine. In contrast, ibogaine had no significant effect on [35S]GTP.gamma.S binding over a similar concn. range. The efficacy of noribogaine as a full .mu.-opioid agonist may explain ibogaine's ability to block the acute signs of opiate withdrawal and its suppressive effects on morphine self-administration.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(noribogaine stimulates naloxone-sensitive GTP.gamma.S binding to G proteins in relation to opioid receptors)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



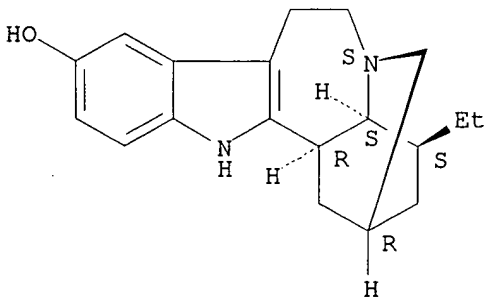
L25 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1998:64806 CAPLUS
DN 128:213189
TI Behavioral and biochemical evidence for a nonessential 5-HT2A component of the ibogaine-induced discriminative stimulus
AU Helsley, Scott; Fiorella, David; Rabin, R. A.; Winter, J. C.
CS Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, NY, 14214-3000, USA
SO Pharmacol., Biochem. Behav. (1998), 59(2), 419-425
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier Science Inc.
DT Journal
LA English
AB In the present investigation, the ability of two known hallucinogens, lysergic acid dimethylamide (LSD) and (-)-2,5-dimethoxy-4-methyl-amphetamine (DOM), to substitute for the ibogaine-induced discriminative stimulus (10 mg/kg IP, 60 min presession) was assessed in Fischer-344 rats. In these subjects, intermediate levels of generalization were obsd. to both agents (LSD, 63%; DOM, 66.4%). This intermediate generalization was completely blocked by pretreatment with the 5-HT2A antagonist pirenpirone, suggesting that the ibogaine-like effects of these agents are mediated by the 5-HT2A receptor. However, pirenpirone did not antagonize ibogaine itself, nor did it antagonize the ibogaine-like effects of harmaline and 12-hydroxyibogamine (noribogaine). To further evaluate the serotonergic properties of ibogaine, in vivo protection assays and in vitro binding assays were employed. Micromolar 5-HT2A affinity was obsd. with ibogaine (92.5 .mu.M), 12-hydroxyibogamine (34.5 .mu.M), and harmaline (42.5 .mu.M). Despite the apparently low affinity of these agents, both ibogaine and harmaline, but not 12-hydroxyibogamine, produced significant protection from receptor alkylation by N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) when given 60 min prior to this alkylating agent. The results of these studies suggest that although ibogaine may produce some of its effects via interactions with 5-HT2A receptors, these do not appear to be essential to the ibogaine-induced discriminative stimulus.
IT **481-88-9**, 12-Hydroxyibogamine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(5-HT2A receptors role in mediating ibogaine and harmaline-induced discriminative stimulus)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



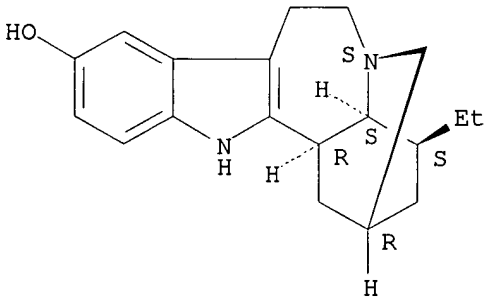
L25 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:679297 CAPLUS
DN 128:266
TI Effects of noribogaine on the development of tolerance to antinociceptive action of morphine in mice
AU Bhargava, Hemendra N.; Cao, Ying-Jun
CS Department of Pharmaceutics and Pharmacodynamics (m/c 865), The University of Illinois at Chicago, Health Sciences Center, 833 South Wood Street, Chicago, IL, 60612, USA
SO Brain Res. (1997), 771(2), 343-346
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier
DT Journal
LA English
AB The effects of noribogaine, a metabolite of ibogaine, on the development of tolerance to the antinociception action of morphine was detd. in male Swiss-Webster mice. Ibogaine is an alkaloid isolated from the bark of the African shrub, Tabernanthe iboga. Morphine tolerance in mice was developed by two different methods. Mice were rendered tolerant to morphine either by s.c. implantation of a pellet contg. 25 mg morphine free base for 4 days or by injecting morphine (20 mg/kg, s.c.) twice a day for 4 days. Placebo pellet implanted mice or vehicle injected mice served as controls. To det. the effect of i.p. administered noribogaine on tolerance development, the drug was injected in the appropriate dose twice a day. In pellet implanted mice, a dose of 20 mg/kg of noribogaine attenuated the tolerance to morphine whereas lower doses had no effect. Similarly, in mice given multiple injections of morphine, noribogaine attenuated tolerance development at 20 and 40 mg/kg doses. Previous studies from this lab. had shown that ibogaine at 40 and 80 mg/kg doses inhibited tolerance to morphine. Because noribogaine could attenuate morphine tolerance at lower doses than ibogaine, it is concluded that the attenuating effect of ibogaine on morphine tolerance may be mediated by its conversion to noribogaine, a more active metabolite.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of noribogaine on development of tolerance to antinociceptive action of morphine in mice)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



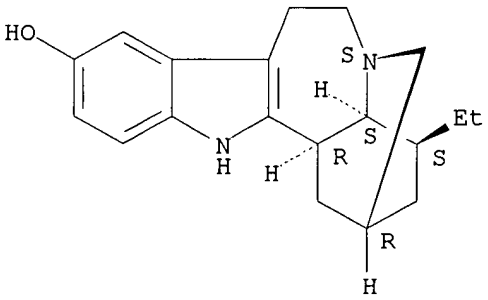
L25 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:646580 CAPLUS
DN 127:341636
TI Time-dependent interactions between iboga agents and cocaine
AU Maisonneuve, Isabelle M.; Visker, Kathleen E.; Mann, Gina L.; Bandarage, Upul K.; Kuehne, Martin E.; Glick, Stanley D.
CS Department of Pharmacology and Neuroscience, A-136, Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208, USA
SO Eur. J. Pharmacol. (1997), 336(2/3), 123-126
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English
AB The purpose of this study was to clarify the effects of iboga agents on cocaine-induced hyperactivity. Both inhibition and enhancement of cocaine-induced activity by ibogaine have been reported. In the present study, rats were treated with either ibogaine (40 mg/kg, i.p.), noribogaine (40 mg/kg, i.p.), 18-methoxycoronaridine (40 mg/kg, i.p.), or saline, 1 or 19 h prior to the administration of cocaine (20 mg/kg, i.p.) or saline. Motor activity was monitored thereafter for 3 h. All three iboga agents had acute inhibitory effects and delayed potentiating effects on cocaine-induced hyperactivity. These time-dependent effects, which could not be attributed to the motor activity induced by the iboga agents alone, account for divergent results reported in the literature.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(time-dependent interactions between iboga agents and cocaine-induced hyperactivity)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



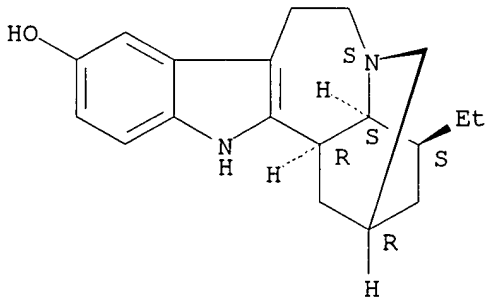
L25 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:521853 CAPLUS
DN 127:215026
TI Sex differences in ibogaine antagonism of morphine-induced locomotor activity and in ibogaine brain levels and metabolism
AU Pearl, S. M.; Hough, L. B.; Boyd, D. L.; Glick, S. D.
CS Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Pharmacol., Biochem. Behav. (1997), 57(4), 809-815
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier
DT Journal
LA English
AB The present study demonstrates that the putative antiaddictive agent ibogaine produces more robust behavioral effects in female than in male rats and that these behavioral differences correlate with higher levels of ibogaine in the brain and plasma of female rats. There were no differences in basal Iocomotor activity between the sexes, and the response of rats to ibogaine differed between the sexes even in the absence of morphine. Five h after receiving ibogaine (40 mg/kg, IP), antagonism of morphine-induced locomotor activity was evident in female but not in male rats. Either 19 h after administration of ibogaine (10-60 mg/kg, IP), or one h after administration of noribogaine (5-40 mg/kg, IP), a suspected metabolite, antagonism of morphine was significantly greater in female than in male rats. Brain and plasma levels of ibogaine (1 h) and noribogaine (5 h), measured by gas chromatog.-mass spectrometry, were greater in females as compared with males receiving the same dose of ibogaine. Levels of both ibogaine and noribogaine were substantially lower at 19 h than at earlier times after ibogaine administration, contrary to a previous study in humans. For both sexes, s.c. administration of ibogaine (40 mg/kg, IP, 19 h) produced greater antagonism of morphine-induced locomotor activity than did a comparable i.p. injection, consistent with previous studies from this lab. demonstrating that the former route of administration produces higher levels of ibogaine in the brain. These data show that there are sex differences in the effects of ibogaine and that this may be due to decreased bioavailability of ibogaine in males as compared to females.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(sex differences in ibogaine antagonism of morphine-induced locomotor activity and ibogaine brain levels and metab.)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:156627 CAPLUS
DN 126:246705
TI Effects of ibogaine and noribogaine on the antinociceptive action of .mu.-, .delta.- and .kappa.-opioid receptor agonists in mice
AU Bhargava, Hemendra N.; Cao, Ying-Jun; Zhao, Guo-Min
CS Department of Pharmaceutics and Pharmacodynamics (M/C 865), The University of Illinois at Chicago, Health Sciences Center, 833 South Wood Street, Chicago, USA
SO Brain Res. (1997), 752(1,2), 234-238
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier
DT Journal
LA English
AB Ibogaine, an alkaloid isolated from the bark of the African shrub, Tabernanthe iboga, has been claimed to decrease the self-administration of drugs of abuse like morphine, cocaine and alc. To det. whether these effects are mediated via opioid receptor systems, the effects of ibogaine and its metabolite, noribogaine on the antinociceptive actions of morphine, U-50,488H and [D-Pen2,D-Pen5]enkephalin (DPDPE) which are .mu.- .kappa.- and .delta.-opioid receptor agonists, resp., were detd. in male Swiss-Webster mice. Administration of morphine (7 or 10 mg/kg, s.c.), U-50,488H (15 or 25 mg/kg, i.p.) or DPDPE (10 .mu.g/mouse, i.c.v.) produced antinociception in mice as measured by the tail-flick test. Ibogaine (10, 20 or 40 mg/kg, i.p.) by itself did not alter the tail-flick latency. The same doses of ibogaine injected 10 min before the opioid drugs did not modify the antinociceptive actions of morphine, U-50,488H or DPDPE. Ibogaine administered 4 h or 24 h prior to morphine injection did not modify the antinociceptive action of the latter. A dose of 40 mg/kg (i.p.) of noribogaine enhanced the antinociceptive activity of morphine (10 mg/kg, s.c.). Similarly, the doses of 40 and 80 mg/kg of noribogaine enhanced the antinociception produced by a smaller dose of morphine (5 mg/kg, s.c.). However, antinociception induced by U-50,488H and DPDPE was not modified by noribogaine (10-40 mg/kg). It is concluded that ibogaine, which has been suggested to decrease the self-administration of cocaine and opiates like heroin in humans, does not produce such an action by interacting directly with multiple opioid receptors. However, the metabolite of ibogaine enhances the antinociception of morphine but not of U-50,488H or DPDPE. Thus, in vivo evidence has been provided for the possible interaction of ibogaine with .mu.-opioid receptor following its metab. to noribogaine.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of ibogaine and noribogaine on antinociceptive action of opioid receptor agonists)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.


HO
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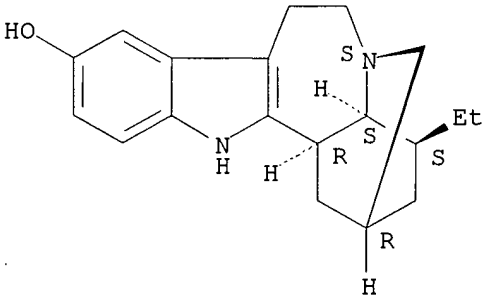
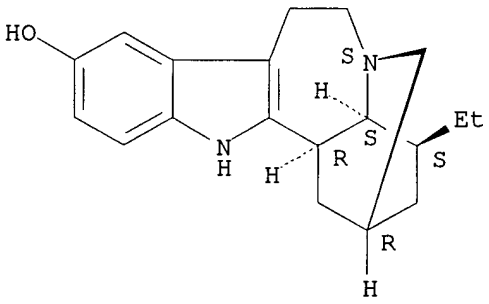
L25 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:102850 CAPLUS
DN 126:207400
TI The effects of noribogaine and harmaline in rats trained with ibogaine as a discriminative stimulus
AU Helsley, Scott; Rabin, Richard A.; Winter, J. C.
CS Dep. of Pharmacology and Toxicology, State University of New York at Buffalo, Buffalo, NY, 14214-3000, USA
SO Life Sci. (1997), 60(9), PL147-PL153
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier
DT Journal
LA English
AB In the present investigation, Fischer-344 rats were trained to discriminate 10.0 mg/kg of ibogaine from water using a pretreatment time of 60 min. Anal. of dose response data generated an ED50 of 4.6 mg/kg. The time course of the ibogaine (10.0 mg/kg) cue was also detd. The stimulus reached a max. level of 94% ibogaine-appropriate responding at the 60-min pretreatment time. This was followed by a time-dependent decrease in ibogaine-appropriate responding. At a pretreatment time of 8 h only 6.4% drug-appropriate responding was obsd. In substitution expts., intermediate generalization was obsd. with a metabolite of ibogaine, 12-hydroxyibogamine [noribogaine] (71.6%) whereas complete generalization was seen with harmaline (83.5%).
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of noribogaine and harmaline in rats trained with ibogaine as discriminative stimulus)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:63998 CAPLUS
DN 126:233451
TI Ibogaine: a potent noncompetitive blocker of ganglionic/neuronal nicotinic receptors
AU Badio, Barbara; Padgett, William L.; Daly, John W.
CS Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0820, USA
SO Mol. Pharmacol. (1997), 51(1), 1-5
CODEN: MOPMA3; ISSN: 0026-895X
PB Williams & Wilkins
DT Journal
LA English
AB Ibogaine noncompetitively blocked (lC50 .apprx. 20 nM) 22NaCl influx through ganglionic-type nicotinic receptor channels of rat pheochromocytoma PC12 cells. The major metabolite O-des-methylibogaine was 75-fold less active, and O-t-butyl-O-des-methylibogaine was 20-fold less active. Ibogaine was relatively weak as a blocker (lC50 .apprx. 2000 nM) of the neuromuscular-type nicotinic receptor channels in human medulloblastoma TE671 cells. The blockade of nicotinic responses by ibogaine was only partially reversible in PC12 cells. In vivo, ibogaine at 10 mg/kg completely blocked epibatidine-elicited antinociception in mice, a response that is mediated by central nicotinic receptor channels. There was no significant blockade of the epibatidine response at 24 h after the administration of 40 mg/kg ibogaine. The blockade of nicotinic channels could contribute to the antiaddictive properties of ibogaine.
IT **481-88-9**, O-Demethylibogaine
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(ibogaine: a potent noncompetitive blocker of ganglionic/neuronal nicotinic receptors)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.

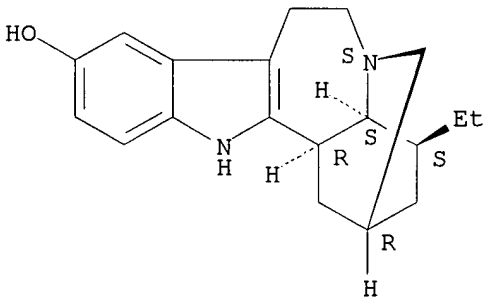


L25 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1997:49269 CAPLUS
DN 126:152816
TI Method of treating chemical dependency using .beta.-carboline alkaloids, derivatives and salts thereof
IN Lotsof, Howard S.
PA NDA International, Inc., USA
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5591738	A	19970107	US 1994-322490	19941014

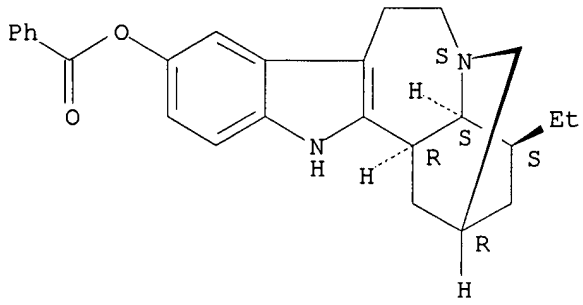
OS MARPAT 126:152816
AB A method of treating a chem. dependency disorder, an abuse syndrome or a combination thereof in a mammal in need thereof, comprises administering (1) an effective amt. of a .beta.-carboline alkaloid, hydrolyzable deriv. or pharmaceutically-acceptable salt thereof, such as harmaline, harmine, tetrahydroharmine, tetrahydronorharman, harmol, harmalol, Et harmol, Pr harmol, iso-Pr harmol, and Bu harmol and (2) an effective amt. of a noribogaine compd.
IT **481-88-9**, Noribogaine **176916-14-6**, O-Benzoylnoribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chem. dependency treatment with .beta.-carboline alkaloids and noribogaine derivs.)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 176916-14-6 CAPLUS
CN Ibogamin-12-ol, benzoate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.


Ph
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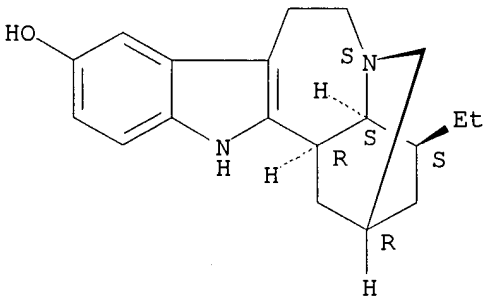
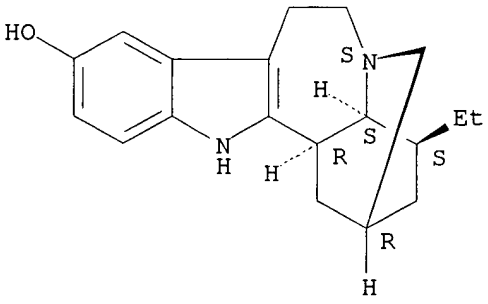
L25 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:726840 CAPLUS
DN 126:54741
TI Ibogaine and noribogaine potentiate the inhibition of adenylyl cyclase activity by opioid and 5-HT receptors
AU Rabin, Richard A.; Winter, Jerrold C.
CS Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, NY, 14214-3000, USA
SO Eur. J. Pharmacol. (1996), 316(2/3), 343-348
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English
AB The effects of the putative anti-addictive compd. ibogaine and its principal metabolite, noribogaine, on adenylyl cyclase activity were detd. in various areas of the rat brain. Neither compd. altered either basal or forskolin-stimulated adenylyl cyclase activities in the frontal cortex, midbrain or striatum. However, in all three brain areas the addn. of ibogaine and noribogaine significantly enhanced inhibition of adenylyl cyclase activity by a maximally effective concn. of morphine. Similarly, both compds. also potentiated the inhibition of hippocampal adenylyl cyclase activity by a maximally effective concn. of 5-hydroxytryptamine (5-HT). Although ibogaine appears to be more potent than noribogaine in augmenting opioid- and 5-HT-mediated inhibition of adenylyl cyclase activity, both compds. appear to be of comparable efficacy. Neither compd., however, modified the inhibitory action of the muscarinic acetylcholine agonist, carbachol, on adenylyl cyclase activity. The present data indicate that ibogaine and noribogaine cause a selective increase in receptor-mediated inhibition of adenylyl cyclase activity. This potentiation may be involved in the pharmacol. actions of these compds.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibogaine and noribogaine potentiate inhibition of adenylyl cyclase activity by opioid and serotonin receptors)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



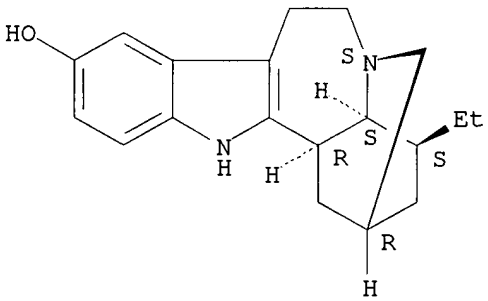
L25 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:710970 CAPLUS
DN 126:139743
TI Facilitation of memory retrieval by the "anti-addictive" alkaloid, ibogaine
AU Popik, Piotr
CS Inst. Pharm., Polish Acad. Sci., Krakow, 31-343, Pol.
SO Life Sci. (1996), 59(24), PL379-PL385
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier
DT Journal
LA English
AB Anecdotal observations in humans indicate that indole alkaloid ibogaine may have antiaddictive properties. It has been suggested that therapeutic action of ibogaine may depend upon facilitated access to the past experiences, purportedly influencing the initiation of drug addiction. To det. if ibogaine may facilitate memory retrieval, rats were trained in the Morris maze spatial navigation task. It has been found that ibogaine (0.25 or 2.5 mg/kg) or O-desmethyl-ibogaine, but not t-Bu ibogaine, administered just before the test trial, facilitated spatial memory retrieval compared to rats receiving placebo treatment. It is concluded that although previously described NMDA receptor antagonistic properties of ibogaine may represent a locus for at least some of its actions, other mechanisms, involving facilitation of memory retrieval may be of importance for its anti-addictive effects.
IT **481-88-9**, Ibogamin-12-ol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(facilitation of memory retrieval by the "anti-addictive" alkaloid, ibogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



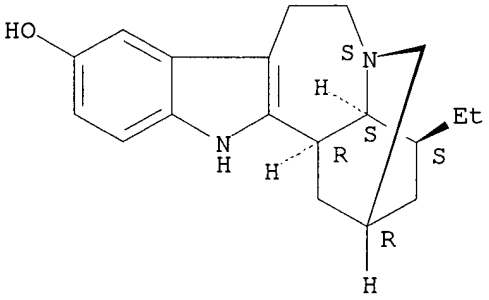
L25 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:692751 CAPLUS
DN 126:26668
TI Modulation of morphine-induced antinociception by ibogaine and noribogaine
AU Bagal, A. A.; Hough, L. B.; Nalwalk, J. W.; Glick, S. D.
CS Department of Pharmacology and Neuroscience, A-136, Albany Medical College, 47 New Scotland Ave., Albany, NY, 12208, USA
SO Brain Res. (1996), 741(1,2), 258-262
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier
DT Journal
LA English
AB The potential modulation of morphine antinociception by the putative anti-addictive agent ibogaine and its active metabolite (noribogaine) was investigated in rats with the radiant heat tail-flick test. Ibogaine pretreatment (40 mg/kg, i.p., 19 h) significantly decreased morphine (4 mg/kg, s.c.) antinociception, with no effects in the absence of morphine. However, co-administration of ibogaine (1-40 mg/kg, i.p.) and morphine (4 mg/kg, s.c.) exhibited a dose-dependent enhancement of morphine antinociception. Co-administration of noribogaine (40 mg/kg, i.p.) and morphine also resulted in an increase in morphine antinociception, while noribogaine pretreatment (19 h) had no effect on morphine antinociception. The results show that ibogaine acutely potentiates morphine antinociception and that noribogaine could be the active metabolite responsible for this effect. However, the inhibitory effects of a 19 h ibogaine pretreatment, which resemble ibogaine-induced inhibition of morphine's stimulant properties, cannot be accounted for by noribogaine.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulation of morphine-induced antinociception by ibogaine and noribogaine)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



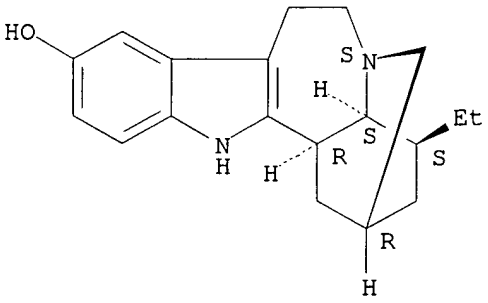
L25 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:572474 CAPLUS
DN 125:238572
TI Pharmacological screen for activities of 12-hydroxyibogamine: a primary metabolite of the indole alkaloid ibogaine
AU Staley, Julie K.; Ouyang, Qinjie; Pablo, John; Hearn, W. Lee; Flynn, Donna D.; Rothman, Richard B.; Rice, Kenner C.; Mash, Deborah C.
CS Dep. Neurol., Univ. Miami Sch. Med., Miami, FL, 33101, USA
SO Psychopharmacology (Berlin) (1996), 127(1), 10-18
CODEN: PSCHDL; ISSN: 0033-3158
DT Journal
LA English
AB The purported efficacy of ibogaine for the treatment of drug dependence may be due in part to an active metabolite. Ibogaine undergoes first pass metab. and is O-demethylated to 12-hydroxyibogamine (12-OH ibogamine). Radioligand binding assays were conducted to identify the potency and selectivity profiles for ibogaine and 12-OH ibogamine. A comparison of 12-OH ibogamine to the primary mol. targets identified previously for ibogaine demonstrates that the metabolite has a binding profile that is similar, but not identical to the parent drug. Both ibogaine and 12-OH ibogamine demonstrated the highest potency values at the cocaine recognition site on the 5-HT transporter. The same rank order (12-OH ibogamine > ibogaine), but lower potencies were obsd. for the [3H]paroxetine binding sites on the 5-HT transporter. Ibogaine and 12-OH ibogamine were equipotent at vesicular monoamine and dopamine transporters. The metabolite demonstrated higher affinity at the kappa-1 receptor and lower affinity at the NMDA receptor complex compared to the parent drug. Quantitation of the regional brain levels of ibogaine and 12-OH ibogamine demonstrated micromolar concns. of both the parent drug and metabolite in rat brain. Drug dependence results from distinct, but inter-related neurochem. adaptations, which underlie tolerance, sensitization and withdrawal. Ibogaine's ability to alter drug-seeking behavior may be due to combined actions of the parent drug and metabolite at key pharmacol. targets that modulate the activity of drug reward circuits.
IT **481-88-9**, 12-Hydroxyibogamine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibogaine metabolite 12-hydroxyibogamine in drug dependence treatment)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



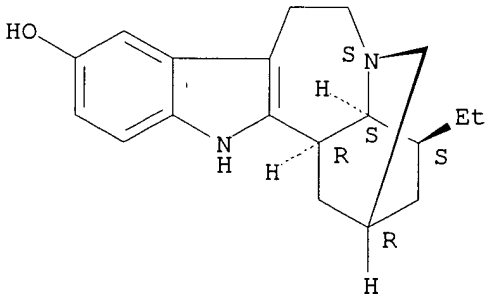
L25 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:490818 CAPLUS
DN 125:238257
TI Effects of ibogaine and noribogaine on phosphoinositide hydrolysis
AU Rabin, Richard A.; Winter, J. C.
CS Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, 102 Farber Hall, Buffalo, NY, 14214-3000, USA
SO Brain Res. (1996), 731(1,2), 226-229
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB The effects of the antiaddictive compd., ibogaine, and its primary metabolite, noribogaine (12-hydroxyibogamine), on phosphoinositide hydrolysis were investigated. Although ibogaine did not alter phosphoinositide turnover in either striatal or hippocampal slices, noribogaine elicited a concn.-dependent increase in the generation of [3H]inositol phosphates. This stimulation was not altered by inclusion of tetrodotoxin, cadmium or .omega.-conotoxin indicating that the increased prodn. of [3H]inositol phosphates was not secondary to a release of one or more neurotransmitters. The present study indicates a stimulation of phosphoinositide hydrolysis by noribogaine may be involved in the behavioral effects of ibogaine.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of ibogaine and noribogaine on phosphoinositide hydrolysis)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:475146 CAPLUS
DN 125:238250
TI Structurally modified ibogaine analogs exhibit differing affinities for NMDA receptors
AU Layer, Richard T.; Skolnick, Phil; Bertha, Craig M.; Bandarage, Upul K.; Kuehne, Martin E.; Popik, Piotr
CS Laboratory of Neuroscience, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA
SO Eur. J. Pharmacol. (1996), 309(2), 159-165
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB Based on both preclin. findings and anecdotal evidence in man, the psychoactive indole alkaloid ibogaine has been suggested to have anti-addictive properties. Previous studies indicate that blockade of NMDA receptors may mediate at least some of the putative anti -addictive actions of ibogaine. The potencies of a series of ibogaine analogs to inhibit (+)-[3-3H]5-methyl-10,11-dihydro-5H-dibenzo-[a,d]cyclohepten-5,10-imine ([3H]MK-801) binding to NMDA receptors were examd. This series of analogs included the putative ibogaine metabolite O-desmethylibogaine, its metab.-resistant analog O-tert-Bu-O-desmethylibogaine, the iboga alkaloids (.+-.)-ibogamine, (.+-.)-coronaridine, tabernanthine, harmaline, and the indolotropanes endo-3-(1-methylindol-2-yl)-8-methyl-8-azabicyclo[3.2.1]octane (RS 075194-190), exo-3-(1-methylindol-2-yl)-8-methyl-8-azabicyclo[3.2.1]octane (RS 075237-190) and endo-3-(indol-2-yl)-8-methyl-8-azabicyclo[3.2.1]octane (RS 025989-190). Among these compds., ibogaine was the most potent inhibitor of [3H]MK-801 binding (Ki = .apprx.1.2 .mu.M), while the compds. with the greatest structural similarity to ibogaine, O -desmethylibogaine and O-t-butyl-O-desmethylibogaine were less potent (Ki = .apprx.5.5 and 179.0 .mu.M, resp.). In morphine-dependent mice, ibogaine, but not O-desmethylibogaine or O-t-butyl-O-desmethylibogaine, attenuated naloxone pptd. withdrawal jumping. These findings are consistent with the hypothesis that inhibition of the expression of morphine dependence by ibogaine is related to its NMDA receptor antagonist properties.
IT **481-88-9**, Ibogamin-12-ol
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ibogaine analog affinity for NMDA receptor and drug dependence inhibition, and O-t-butyl-O-desmethylibogaine prepn.)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.

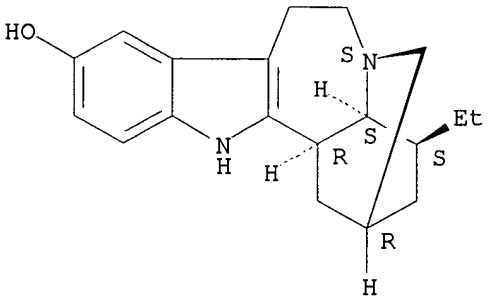


L25 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:321083 CAPLUS
DN 124:333123
TI Noribogaine compounds for treating chemical dependency in mammals
IN Mash, Deborah C.; Sanchez-Ramos, Juan; Hearn, W. Lee
PA Nda International, Inc., USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9603127	A1	19960208	WO 1995-US9136	19950725
	W: CA, MX				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9646132	A1	19960419	AU 1996-46132	19950725
	EP 804200	A1	19971105	EP 1995-927295	19950725
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US 6348456	B1	20020219	US 1996-727123	19961008
PRAI	US 1994-280187	A	19940725		
	WO 1995-US9136	W	19950725		

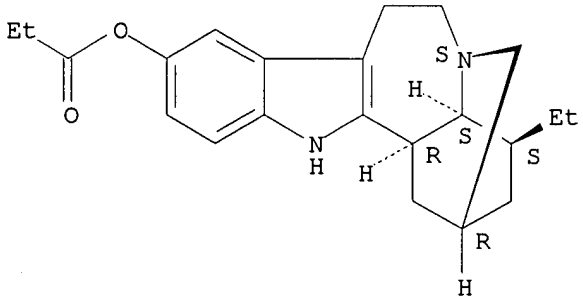
OS MARPAT 124:333123
AB An essentially pure noribogaine compd., particularly noribogaine or a hydrolyzable deriv. thereof, reduces craving for addictive substances and is longer acting than ibogaine.
IT **481-88-9**, 12-Hydroxyibogamine **176916-13-5**, O-Acetylnoribogaine **176916-14-6**, O-Benzoylnoribogaine **176916-15-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noribogaine compds. for treating chem. dependency)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



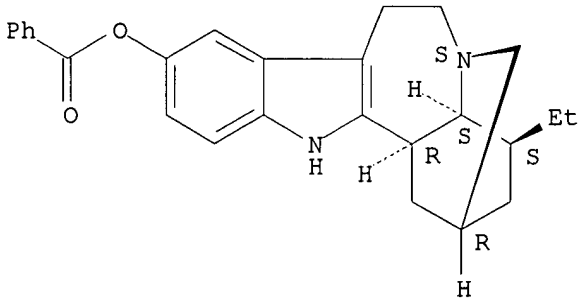
RN 176916-13-5 CAPLUS
CN Ibogamin-12-ol, propanoate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



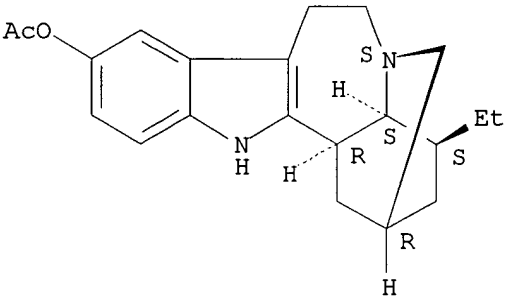
RN 176916-14-6 CAPLUS
CN Ibogamin-12-ol, benzoate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



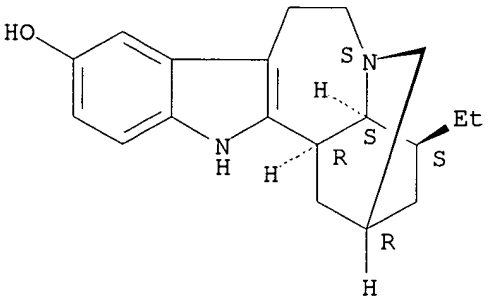
RN 176916-15-7 CAPLUS
CN Ibogamin-12-ol, acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



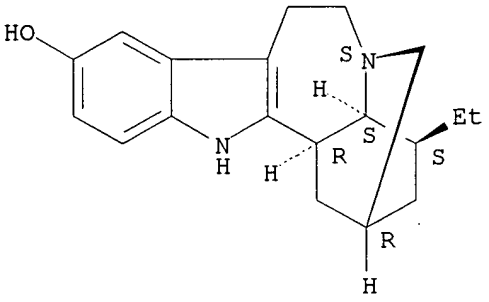
L25 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1996:214023 CAPLUS
DN 124:279016
TI Ibogaine-like effects of noribogaine in rats
AU Glick, S. D.; Pearl, S. M.; Cai, J.; Maisonneuve, I. M.
CS Department of Pharmacology and Neuroscience, Albany Medical College, New Scotland Avenue, Albany, NY, 12208, USA
SO Brain Res. (1996), 713(1,2), 294-7
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Ibogaine is a naturally occurring alkaloid that has been claimed to be effective in treating addiction to opioids and stimulants; a single dose is claimed to be effective for 6 mo. Analogously, studies in rats have demonstrated prolonged (one or more days) effects of ibogaine on morphine and cocaine self-administration even though ibogaine is mostly eliminated from the body in several hours. These observations have suggested that a metabolite may mediate some of the effects of ibogaine. Recently, noribogaine was identified as a metabolite of ibogaine. Accordingly, the present study sought to det., in rats, whether noribogaine had pharmacol. effects mimicking those of ibogaine. Noribogaine (40 mg/kg) was found to decrease morphine and cocaine self-administration, reduce the locomotor stimulant effect of morphine, and decrease extracellular levels of dopamine in the nucleus accumbens and striatum. All of these effects were similar to effects previously obsd. with ibogaine (40 mg/kg); however, noribogaine did not induce any ibogaine-like tremors. The results suggest that noribogaine may be a mediator of ibogaine's putative anti-addictive effects.
IT **481-88-9**, Noribogaine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noribogaine decreases cocaine and morphine self-administration and extracellular levels of dopamine in brain)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



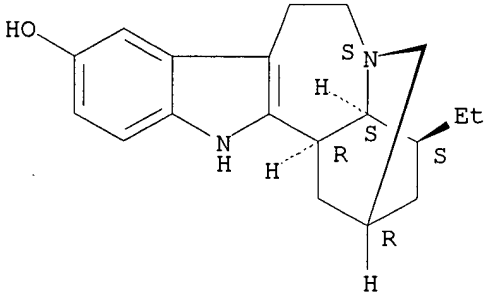
L25 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:850984 CAPLUS
DN 123:275065
TI Identification and quantification of ibogaine and an o-demethylated metabolite in brain and biological fluids using gas chromatography-mass spectrometry
AU Hearn, William L.; Pablo, John; Hime, George W.; Mash, Deborah C.
CS Metro-Dade County Medical Examiner's Dep., Univ. of Miami School of Medicine, Miami, FL, 33136, USA
SO J. Anal. Toxicol. (1995), 19(6), 427-34
CODEN: JATOD3; ISSN: 0146-4760
DT Journal
LA English
AB This report describes a sensitive method for quantitating ibogaine and a single major metabolite in biol. fluids and brain tissue. We identified the metabolite as 12-hydroxy-ibogamine (12-OH-ibogamine or noribogaine) by full-scan, electron-impact gas chromatog.-mass spectrometry (GC-MS). Ibogaine, 12-OH-ibogamine, and o-(methyl)-ibogaine-d3 (ibogaine-d3) internal std. were isolated by solvent extn. under basic conditions. The resulting org. ext. was evapd. to dryness, and the residue was derivatized at room temp. with Et iodide in the presence of tri-Me anilinium hydroxide in DMSO. The reaction was terminated by acidification and washed with org. solvents to remove impurities. The aq. phase was then alkalinized and reextd. The org. ext. was concd. and analyzed by GC-MS. Quantitation was based upon the ratios of the mol. ions at m/z 310 for ibogaine, m/z 313 for ibogaine-d3, and m/z 324 for 12-OH-ibogamine Et ether. The limit of detection was 5 ng/mL for both ibogaine and derivatized 12-OH-ibogamine, and limits of quantitation were between 5 and 10 ng/mL for all matrixes tested. Calibration curves were linear in the range of 5-1000 ng/mL or ng/g for both analytes.
IT **481-88-9**, Noribogaine
RL: ANT (Analyte); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(ibogaine and noribogaine detn. in brain and biol. fluids by gas chromatog.-mass spectrometry)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



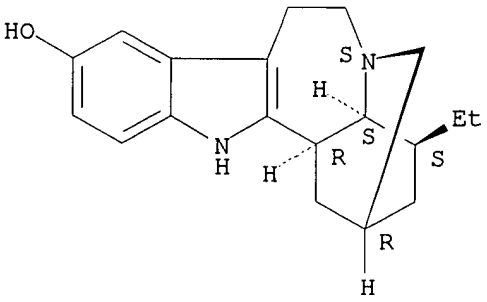
L25 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:850978 CAPLUS
DN 123:275064
TI Determination of ibogaine and 12-hydroxy-ibogamine in plasma by gas chromatography-positive ion chemical ionization-mass spectrometry
AU Alburges, Mario E.; Foltz, Rodger L.; Moody, David E.
CS Center for Human Toxicology, Univ. of Utah, Salt Lake City, UT, 84112, USA
SO J. Anal. Toxicol. (1995), 19(6), 381-6
CODEN: JATOD3; ISSN: 0146-4760
DT Journal
LA English
AB Ibogaine, an indolamine deriv., is currently being investigated as a potential agent in the treatment of stimulant and opiate addiction. We developed a rapid, sensitive, and specific method for the anal. of ibogaine and its putative active metabolite, 12-hydroxy-ibogamine (12-OH-ibogamine). This assay employs a one-step basic extn. with Bu chloride-acetonitrile (4:1), followed by derivatization of the metabolite using N-methyl-N-(tert-butyldimethylsilyl)-trifluoroacetamide. The derivatized exts. were analyzed by capillary gas chromatog.-pos. ion chem. ionization-mass spectrometry. The ions monitored were at m/z 311, 314, and 411, which correspond to the protonated mols. (MH+) for ibogaine, ibogaine-d3, and 12-OH-ibogamine.cntdot.tert-butyldimethylsilyl, resp. Linear std. curves were obtained over the concn. range of 10-1000 ng/mL (av. r2, 0.995 for ibogaine and 0.992 for 12-OH-ibogamine; n = 3). Limits of quantitation were 10 ng/mL. The interrun and intrarun coeffs. of variation for the assay of ibogaine at 25, 100, and 300 ng/mL ranged from 2.9 to 8.8%. We also established the extn. and chromatog. conditions to monitor the 12-hydroxylated metabolite. A suitable internal std. was not yet obtained so the method could only provide semiquant. information for 12-OH-ibogamine. Chem. stability studies of these analytes indicated that ibogaine and 12-OH-ibogamine were stable in a human plasma matrix at room temp. for a period of at least 1 wk.
IT **481-88-9**, 12-Hydroxy-ibogamine
RL: ANT (Analyte); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(ibogaine and hydroxyibogamine detn. in plasma by gas chromatog.-pos. ion chem. ionization-mass spectrometry)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



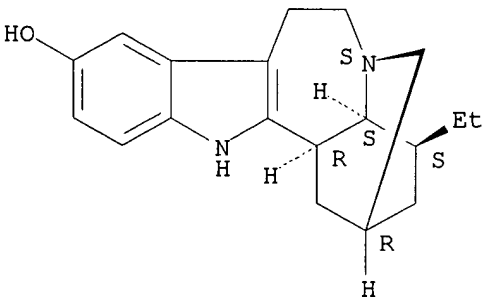
L25 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:628238 CAPLUS
DN 123:74687
TI Properties of ibogaine and its principal metabolite (12-hydroxyibogamine) at the MK-801 binding site of the NMDA receptor complex
AU Mash, D. C.; Staley, J. K.; Pablo, J. P.; Holohean, A. M.; Hackman, J. C.; Davidoff, R. A.
CS Department of Neurology (D4-5), PO Box 016960, University of Miami School of Medicine, Miami, FL, 33101, USA
SO Neurosci. Lett. (1995), 192(1), 53-6
CODEN: NELED5; ISSN: 0304-3940
DT Journal
LA English
AB The putative anti-addiction alkaloid ibogaine and its principal metabolite 12-hydroxyibogamine appear to act at the (+)-5 methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-10-imine maleate (MK-801) binding site in the N-methyl-D-aspartate (NMDA)-receptor cation channel. This conclusion is based on findings that both compds. competitively displaced specific [3H]MK-801 binding to membranes from postmortem human caudate and cerebellum and from frog spinal cord. Ibogaine was 4-6-fold more potent than its metabolite and both compds. were less potent (50-1000-fold) than MK-801 binding to the NMDA receptor. In addn., ibogaine (100 .mu.M) and 12-hydroxyibogamine (1 mM) blocked (85-90% of control) the ability of NMDA (100 .mu.M, 5 s) to depolarize frog motoneurons in the isolated frog spinal cord. The prevention of NMDA-depolarizations in frog motoneurons showed use-dependency and was very similar to the block produced by MK-801. In view of the abilities of MK-801 to affect the responses to addictive substances in pre-clin. investigations, our results are compatible with the idea that the ability of ibogaine and 12-hydroxyibogamine to interrupt drug-seeking behavior may, in part, result from their actions at the MK-801 binding site.
IT **481-88-9**, Ibogamin-12-ol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention of drug-seeking by ibogaine and hydroxyibogamine and role of MK-801 binding site of the NMDA receptor complex)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



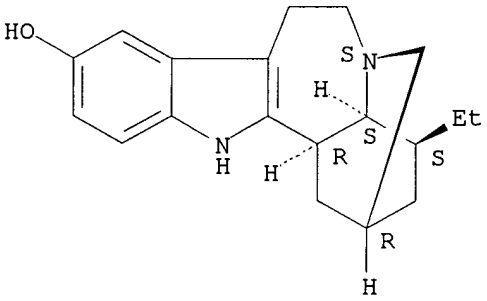
L25 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:621179 CAPLUS
DN 123:47718
TI Identification of a primary metabolite of ibogaine that targets serotonin transporters and elevates serotonin
AU Mash, Deborah C.; Staley, Julie K.; Baumann, Michael H.; Rothman, Richard B.; Hearn, W. Lee
CS Dep. Neurology, Univ. Miami School Medicine, Miami, FL, 33136, USA
SO Life Sci. (1995), 57(3), PL45-PL50
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB Ibogaine is a hallucinogenic indole with putative efficacy for the treatment of cocaine, stimulant and opiate abuse. The purported efficacy of ibogaine following single dose administrations has led to the suggestion that a long-acting metabolite of ibogaine may explain in part how the drug reduces craving for psychostimulants and opiates. We report here that 12-hydroxyibogamine, a primary metabolite of ibogaine, displays high affinity for the 5-HT transporter and elevates extracellular 5-HT. In radioligand binding assays, 12-hydroxyibogamine was 50-fold more potent at displacing radioligand binding at the 5-HT transporter than at the DA transporter. Ibogaine and 12-hydroxyibogamine were equipotent at the dopamine transporter. In vivo microdialysis was used to evaluate the acute actions of ibogaine and 12-hydroxyibogamine on the levels of DA and 5-HT. Administration of 12-hydroxyibogamine produced a marked dose-related elevation of extracellular 5-HT. Ibogaine and 12-hydroxyibogamine failed to elevate DA levels in the nucleus accumbens over the dose range tested. The elevation in synaptic levels of 5-HT by 12-hydroxyibogamine may heighten mood and attenuate drug craving. The effects of the active metabolite on 5-HT transmission may account in part for the potential of ibogaine to interrupt drug-seeking behavior in humans.
IT **481-88-9**, 12-Hydroxyibogamine
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(hydroxyibogamine as ibogaine metabolite that targets serotonin transporters and elevates serotonin)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



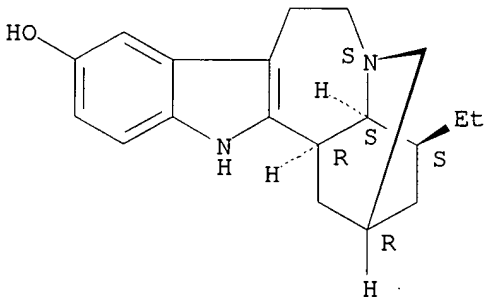
L25 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:608544 CAPLUS
DN 123:74811
TI Ibogaine and its congeners are .sigma.2 receptor-selective ligands with moderate affinity
AU Bowen, Wayne D.; Vilner, Bertold J.; Williams, Wanda; Bertha, Craig M.; Kuehne, Martin E.; Jacobson, Arthur E.
CS Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SO Eur. J. Pharmacol. (1995), 279(1), R1-R3
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB Ibogaine (12-methoxyibogamine) exhibited moderate affinity for .sigma.2 sites (Ki = 201 nM) and low affinity for .sigma.1 sites (Ki = 8554 nM), thus showing 43-fold selectivity for .sigma.2 receptors. Tabernanthine (13-methoxyibogamine) and (.+-.)-ibogamine had .sigma.2 Ki = 194 nM and 137 nM, resp. However, they showed 3- to 5-fold higher .sigma.1 affinity compared to ibogaine, resulting in about 14-fold selectivity for .sigma.2 sites over .sigma.1. A potential ibogaine metabolite, O-des-methyl-ibogaine, had markedly reduced .sigma.2 affinity relative to ibogaine (Ki = 5,226 nM) and also lacked significant affinity for .sigma.1 sites. (.+-.)-Coronaridine ((.+-.)-18-carbomethoxyibogamine) and harmaline (1-methyl-7-methoxy-3,4-dihydro-.beta.-carboline) lacked significant affinity for either .sigma. subtype. Thus, .sigma.2 receptors could play a role in the actions of ibogaine.
IT **481-88-9**, Ibogamin-12-ol
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ibogaine and its congeners are .sigma.2 receptor-selective ligands with moderate affinity)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1995:448716 CAPLUS
DN 122:256172
TI Radioligand-binding study of noribogaine, a likely metabolite of ibogaine
AU Pearl, Sandra M.; Herrick-Davis, Katherine; Teitler, Milton; Glick, Stanley D.
CS Department of Pharmacology and Neuroscience, A-136, Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208, USA
SO Brain Res. (1995), 675(1,2), 342-4
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Radioligand-binding studies were performed to ascertain the actions of noribogaine, a suspected metabolite of ibogaine, on opioid receptors in calf brain cortex and caudate. Consistent with previous results, ibogaine showed highest affinity for .kappa. opioid receptors (Ki = 3.77 .mu.M), less affinity for .mu. receptors (Ki = 11.04 .mu.M) and no affinity for .delta. receptors (Ki >100 .mu.M). Noribogaine showed a higher affinity than ibogaine for all of the opioid receptors: .kappa. Ki = 0.96 .mu.M, .mu. Ki = 2.66 .mu.M and .delta. Ki = 24.72 .mu.M. These data suggest that noribogaine is active in vivo and that it may contribute to ibogaine's pharmacol. effects.
IT **481-88-9**, Ibogamin-12-ol
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(binding of noribogaine and ibogaine to brain opioid receptor subtypes)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2002 ACS
AN 1972:522079 CAPLUS
DN 77:122079
TI Cerebral pharmacokinetics of tremor-producing harmala and iboga alkaloids
AU Zetler, G.; Singbartl, G.; Schlosser, Lucie
CS Inst. Pharmakol., Med. Akad. Luebeck, Luebeck, Ger.
SO Pharmacology (1972), 7(4), 237-48
CODEN: PHMGBN
DT Journal
LA English
AB With the exception of harmalol-HCl, which was effective only when injected intracerebrally, all the other 8 alkaloids tested produced tremor in mice when given s.c. The 4 most active compds. and their ED50 values were tabernanthine (I) [83-94-3] (1.4 mg/kg), ibogaline [482-18-8] (2.6 mg/kg), harmaline [304-21-2] (3.2 mg/kg), and harmine-HCl [17018-99-4] (3.9 mg/kg). Kinetics of evasion from brain were first-order functions with most drugs, but revealed for harmalol and ibogaline 2 and 3 compartments, resp. Tremor-producing activity was much more influenced by chem. structure than by lipid soly.
IT **481-88-9**
RL: BIOL (Biological study)
(tremor from, metabolism by brain in relation to)
RN 481-88-9 CAPLUS
CN Ibogamin-12-ol (9CI) (CA INDEX NAME)

Absolute stereochemistry.